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EXPERIMENTAL DATA FOR ESTABLISHING MAXIMUM PERMISSIBLE CONCENTRATIONS OF TILLAM IN THE AIR OF WORKING AREAS

[Eksperimental'nye dannye k obosnovaniyu predel'no dopustimoy kontsentratsii tillama v vozdukhe rabockey zony]

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EXPERIMENTAL DATA FOR ESTABLISHING MAXIMUM PERMISSIBLE CONCENTRATIONS OF TILLAM IN THE AIR OF WORKING AREAS

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ABSTRACT. Inhalation and skin tests revealed low toxicity of the herbicide tillam. Local irritating effect is moderate, toxicity is low in skin application and cumulative properties are weak. No reproductive changes were noted. The recommended maximum permissible concentration in air is 1 mg/m^3.

Tillam is a herbicide used in the cultivation of sugar beets by injecting it into the soil. The chemically pure preparation is a light liquid with a weak odor. It dissolves poorly in water (92 mg/l at 25°). Its volatility is 0.0109 g/m^3. The preparation is manufactured in the form of a concentration of emulsion (CE) containing over 60% tillam, a solvent (light oil) and an emulsifier of the polyethylene glycol type, as well as in granulated form (N. A. Mel'nikov).

Tests were conducted on animals of both sexes: white mice (weighing 18-22 g), rats (140-170 g), cats (1.5-2.5 kg) and rabbits (1.6-2 kg). A 76.8% CE of tillam was used. Doses and concentrations were calculated according to effective start. Inhalation toxicity was studied in a chamber for dynamic inoculation of the animals with water aerosols. The amount of tillam in the breathing zone (aerosol and vapors) was determined by the colorimetric method developed at the Institute by E. I. Voloshina (sensitivity--5 micrograms per analyzed volume). Criteria of the effect of tillam were: the behavior of the animals, body weight dynamics, relative weight of internal organs and their pathomorphological changes,[1] the blood profile, phagocytic activity of neu-

[1] Pathologomorphological research conducted with Prof. M. B. Rappoport.

trophils, functional indices of the kidneys (diuresis, specific weight of urine, amount of protein in the urine, and amount of rest nitrogen in the blood). In view of the fact that disturbance of oxidation processes is very important in the toxicodynamics of tillam (G. A. Voytenko et al.), we determined the amount of pyroracemic (Friedemann method), a-ketoglutaric and lactic (Dische and Lasic) acids contained in the blood, the activity of cytochromoxidase (Straus), succino-dehydrogenase (Kun and Abood) and lactico-dehydrogenase (Sevela and Tovarek) in liver tissue. We studied the gonadotoxic and embryotoxic effect of the herbicide in tests on white rats using the ordinary methods, as several carbamates and dithiocarbamates have this effect (L. V. Martson; Smally and Curtis, and others). Statistically reliable measurements were made of these indices ($P < 0.05$).

No pronounced variations of the specific sensitivity of the animals to the effect of tillam were found: LD_{50} (according to effective start) is 750 mg/kg for white mice, 1125 mg/kg for white rats; the threshold of local effect is 750 mg/kg for cats.

The local irritating effect of CE of tillam was moderate; with single and multiple (over a period of 2 months) application of chemically pure preparations to the skin of rabbits and injection into the conjunctival sac, the effect of the substance was weak.

The toxicity of tillam in application to the skin is comparatively low; LD_{50} for rats is 2 g/kg; in a dose of 1.5 g/kg the herbicide causes death to a portion of the rabbits. Cumulative ability of the toxic action of tillam is weak; the coefficient of cumulation under the effect of 1/10 LD_{50} is over 5, the administration of 1/20 LD_{50} (total dose 4.2 LD_{50}) does not lead to death of the animals.

We studied the toxicity of tillam penetrating through the respiratory organs in single and multiple tests during 4-hour exposure.

The threshold concentration of the herbicide in single action (9 mg/m^3) is 40 times lower than that causing death to one animal, which implies a

broad zone of toxic effect of the preparation.

In the first series of tests 6 rats were subjected to inoculation with tillam for a period of 40 days in a concentration of 42 ± 3.4 mg/m^3, which was toxic. 5 cats and 32 rats were subjected to tillam in a concentration of 4.7 ± 0.5 mg/m^3 for a period of 4 months. No obvious signs of intoxication or weight changes were detected. Two weeks after the start of the test the phagocytic activity of neutrophils was reduced in the cats. The phagocytic index decreased from 1.4 to 0.67. In 2 and 3 months the phagocytic activity of the neutrophils remained low (42-56%), by the end of the test it was approaching the normal level. Acid resistance of erythrocytes was reduced for 1 to 4 months--acid erythrograms shifted to the left. Amounts of pyroracemic and lactic acid in the blood by the end of the test were reduced. In 2 and 4 weeks a slight (13-23%) increase was noted in the level of rest nitrogen in the blood and urea in the urine. The amount of residual nitrogen contained in the blood was also slightly increased after 8 weeks (at that time albuminuria was noted) and until completion of the chronic test. In the liver of white rats killed after the effect was terminated, the activity of a-ketoglutarotoxidase and pyruvate dehydrogenase was reduced (to 16% and 35% respectively). The amount of pyroracemic acid in the blood increased to 27%. Changes in the internal organs of the animals were noted which were reversible in character (weak hemodynamic and dystrophic disorders). The character and dynamics of changes under the influence of tillam in a concentration of 4.7 mg/m^3 leads us to consider it as threshold for cats and rats in chronic test. Therefore, the chronic effect zone of tillam is 2.

In tests with preliminary administration of 1/100 LD_{50} of tillam for 2 months to sexually immature white rats of both sexes, no gonadotoxic effect was evident. In males no changes were noted in the spermatogenetic index, the number of spermatogonia, percent of sloughed embryonic epithelium, the period of mobility or total number of speratozoons. In females, the estrus cycle proceeded normally. Ability of the animals to reproduce was not dis-

turbed, the development of baby rats (observed for 2 months) did not differ from the control. The administration of 1/20 LD_{50} of tillam to rats during the entire period of pregnancy did not affect its course. Indices of embryo mortality did not differ from those in control animals. The number of baby rats per litter and their development for 2 months did not essentially differ from the control.

On the basis of these data and their comparison with a study of structurally-related pesticides, the maximum permissible concentration of tillam in the air of work areas (vapors and aerosol) is recommended to be 1 mg/m^3; it has been accepted by the Ministry of Public Health of the USSR.

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